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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/724,409 | 11/28/2000 | Clay B. Siegall | 9632-014 | 9908 |

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| EXAMINER | |
|---|---|
| CANELLA, KAREN A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |

DATE MAILED: 03/28/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/724,409 | Siegall et al |
| **Examiner** | **Art Unit** |
| Karen Canella | 1642 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *10-20* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *10-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4*
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

## DETAILED ACTION

1. Claims 10-20 are pending and examined on the merits.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 16 recites "reverse complement" . It is not clear if applicant is intending to actually claim the complementary sequence in reverse polarity, ie, the coding sequence with the 3' to 5' orientation flipped to a 5' to 3' orientation as in the case of a retropeptide. For purpose of examination claim 16 will be read simply as the "complement".

### *Claim Rejections - 35 USC § 102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by any of Tillman et al (J Exp Med, 1992, Vol. 176, pp. 761-779) or Hatano (Accession Number D50136, 1997) or Allessandrini et al (Mol Cell Biol, 1991, Vol. 11, pp. 2096-2107). Claim 10 is drawn in part to an isolated nucleic acid comprising SEQ ID NO:12, SEQ ID NO:13 or SEQ ID NO:15.

Tillman et al disclose an isolated nucleic acid comprising SEQ ID NO:12 as evidenced by Accession Number MDIGKVBJ. Hatano disclose an isolated nucleic acid comprising SEQ ID NO:13 as evidenced by Accession Number D50136. Allessandrini et al disclose an isolated nucleic acid comprising SEQ ID NO:15 as evidenced by Accession Number MUSIGAAA.

6. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by any of Chen et al (J Biol Chem, 1987, Vol. 262, pp. 13579-13583) or Randen et al (Eur J of Immunol, 1993, Vol. 23, pp. 1220-1225) or Singh et al (Lung Research, 1991, Vol. 17, pp. 59-567) Claim 11 is drawn in part to an isolated nucleic acids encoding a protein comprising SEQ ID NO:4, SEQ ID NO:8, or SEQ ID NO:10.

Chen et al disclose an isolated nucleic acid encoding a protein comprising SEQ ID NO:4 as evidenced by Accession Number C29380. Randen et al disclose an isolated nucleic acid encoding a protein as comprising SEQ ID NO:8 evidence by Accession Number S69899. Singh et al disclose an isolated nucleic acid encoding a protein comprising SEQ ID NO:10 as evidenced by Accession Number A61522.

### *Claim Rejections - 35 USC § 103*

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 10-14 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braesch-Anderson et al (Journal of Immunological Methods, 1986, vol. 94, pp. 145-151) in view of deBoer (US 5,677,165). The claims are drawn to isolated nucleic acids encoding a protein which competes for binding to CD40 receptor with monoclonal antibody S2C6 and increases the binding of CD40L to CD40 receptor by at least 45%. Claim 12 is drawn to isolated nucleic acids encoding a protein comprising the heavy chain variable domain of monoclonal antibody S2C6 and a human constant region. Claims 17 and 18 are drawn to recombinant cells comprising the claimed nucleic acids. Claims 19 and 20 are drawn to a method of producing a protein comprising the expression of said recombinant cells.

Braesch-Anderson et al teach the hybridoma secreting the S2C6 monoclonal antibody, said hybridoma having the inherent property of comprising the claimed nucleic acids. Koho et al do not teach an isolated nucleic acid encoding the variable heavy chain of the S2C6 antibody and a human constant region or recombinant cells expressing the claimed nucleic acid sequences, recombinant cell comprising said isolated nucleic acids or a method of producing the protein by mens of recombinant expression in a host cell..

DeBoer teaches the humanized monoclonal antibodies of 5D12, 3A8 and 3C6 which bind to CD40. DeBoer teaches how to obtain the mRNA encoding the monoclonal antibody, and insertion of the nucleic acids encoding the murine variable regions into nucleic acids encoding a human framework region, recombinant cells comprising the isolated nucleic acid encoding the

anti-CD40 humanized monoclonal antibodies and method of producing the humanized monoclonal antibodies comprising recombinant expression of said nucleic acids..

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to isolate the nucleic acid encoding the S2C6 monoclonal antibody from the hybridoma secreting the S2C6 antibody and to make a humanized S2C6 antibody. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Braesh-Anderson et al on the ability of the S2C6 antibody to bind to proliferating B-cells and bladder carcinomas and the teachings DeBoer on methods of obtaining the mRNA encoding a anti-CD40 antibody and methods to humanize antibodies, as well as advantages of using humanized murine antibodies versus murine antibodies in the treatment of human diseases.

9. Claims 10, 11, 13, 14, 16-20 are ejected under 35 U.S.C. 103(a) as being unpatentable over Katira et al (Workshop Panel Report in: Schlossman et al, Leukocyte Typing, Vol. V, p. 547) in view of deBoer (US 5,677,165)., The claims are drawn to isolated nucleic acids encoding a protein which competes for binding to CD40 receptor with monoclonal antibody S2C6 and increases the binding of CD40L to CD40 receptor by at least 45%. Claims 17 and 18 are drawn to recombinant cells comprising the claimed nucleic acids. Claims 19 and 20 are drawn to a method of producing a protein comprising the expression of said recombinant cells.

Katira et al teach a hybridomas secreting the 5C3 monoclonal antibody which competes for binding with S2C6 for CD40 receptor and increases the binding of CD40 ligand to CD40 receptor by at least 45% (Pound et al, Table 1). Katira et al do not teach recombinant cells comprising said isolated nucleic acids, nor a method of producing a protein comprising the expression of said nucleic acids in recombinant cells.

DeBoer et al teach the humanized monoclonal antibodies of 5D12, 3A8 and 3C6 which bind to CD40. DeBoer teaches how to obtain the mRNA encoding the monoclonal antibody, and

insertion of the nucleic acids encoding the murine variable regions into nucleic acids encoding a human framework region.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to isolate the nucleic acids encoding the 5C3 antibody from the hybridoma secreting the 5C3 antibody, to humanize the 5C3 monoclonal antibody and to recombinantly express the isolated nucleic acids for the production of protein. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of DeBoer on methods of humanizing antibodies, and the efficacy of humanized anti-CD40 monoclonal antibodies versus murine antibodies in the treatment of human diseases (column 4, lines 14-19). Neither Katira et al nor Pound et al disclose the nucleic acids encoding the 5C3 monoclonal antibody, however, it is reasonable to assume that the nucleic acids encoding the 5C3 antibody would comprise similar CDR regions as the claimed antibody, and thus it would be reasonable to conclude said hybridoma would comprise said claimed nucleic acids. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

10. Claims 10-20 rejected under 35 U.S.C. 103(a) as being unpatentable over Braesch-Anderson et al (Journal of Immunological Methods, 1986, vol. 94, pp. 145-151) and deBoer (US 5,677,165) as applied to claim 10-14 and 16-20 in section 8 above, and further in view of Francisco et al (Journal of biological chemistry, 1997, vol. 272, pp. 24165-24169). For the reasons set forth in section 8, above, the combination of Braesch-Anderson and deBoer render obvious the embodiments of claims 10-14 and 16-20. Claim 15 is drawn to an isolated nucleic

acid encoding a fusion protein comprising SEQ ID NO:2, SEQ ID NO:7 and the amino acid sequence of bryodin.

Francisco et al teach a single-chain anti-CD40 immunotoxin comprising bryodin-1.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the variable regions of the S2C6 antibody for the variable region of the G28.5 antibody. In the fusion protein comprising bryodin-1. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Francisco et al on the efficacy of administering anti-CD40 immunotoxins to humans in the treatment of non-Hodgkin's lymphoma and multiple myeloma.

***Conclusion***

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Patent Examiner, Group 1642
March 25, 2002

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